

10/588553**IAP11 Rec'd PCT/PTO 07 AUG 2006****PIPETTE VERIFICATION DEVICE AND
PIPETTE FITTED WITH THE SAME****Field of the Invention**

- 5 The present invention relates to liquid dispensing systems capable of delivering, with great precision, very small volumes, typically from 1 nanolitre to several millilitres.

 The invention concerns, more particularly, a pipette verification device and a pipette fitted with the same.

10 **Background of the Invention**

- The pipettes currently available on the market, often called micropipettes, are syringes including a cylinder extended by a shaft and a dispensing tip and a piston sliding in the cylinder. This piston can be actuated, manually or by a motor, over a travel determined by the operator using a
- 15 suitable counter.

- During operation, the piston is pushed down to its end position, the dispensing tip of the shaft is dipped into the liquid to be sampled, then the piston is moved up by a distance corresponding to the volume of liquid displayed on the counter. The upward movement of the piston causes the
- 20 desired volume of liquid to be aspirated into the tip, said liquid being then able, via another downward movement of the piston, to be discharged into a target reserved therefor.

- Pipettes of this type, both manual and motorized, are disclosed, for example, in US Patents 5 983 733, 6 170 343 and 6 254 832. Multishaft
- 25 pipettes are also disclosed, for example, in US Patents 4 779 467 and 5 456 879.

- According to the requirements of the "Good Laboratory and Manufacturing Processes" applied to pipettes, monitoring and recording measures should be taken regarding the volume of liquid dispensed.
- 30 Malfunction of a pipette means that all the tests carried out with the instrument have to be reconsidered, which constitutes an expensive operation.

 Moreover, the quality of a pipette's performance necessarily falls off over time. After a certain number of operations, each pipette has to undergo a

preventive maintenance procedure. Operators thus have not only to determine after how many pipetting operations such maintenance has to be carried out, but also keep pipette calibration records.

Finally, account has to be taken of the fact that the accuracy of the
5 pipette also depends on the operator, who may be more or less skilled and who determines the temperature of the instrument, which influences the volume of aspirated air.

Summary of the invention

It is an object of the present invention to meet the quality control
10 requirements that have just been mentioned.

More precisely, the invention concerns a verification device for a pipette with a piston for aspirating then dispensing, using a shaft, a determined volume of liquid. This device essentially includes:

- first means for supplying a displaced volume measurement,
15 comparing this measurement to a desired value and generating an indication of the difference between the measured volume and said desired value; and
- second means, responding to said first means, for delivering an information relating to said indication.

20 The device defined hereinbefore also has the following main features:

- Said first means include a sensor capable of supplying a pressure measurement at two points of the shaft, and a microprocessor programmed to calculate, from this measurement, the volume displaced in the shaft, to verify that
25 this volume corresponds to the desired volume value and to generate an indication relating to said verification.
- The sensor is capable of supplying, in addition, a measurement of the temperature in the shaft.
- Said second means include a display and, preferably, an
30 acoustic alarm.

- Said second means include a transceiver capable of making the microprocessor communicate with a control and recording unit.
- 5 - The microprocessor is programmed to store instructions that are sent thereto by said unit and to send thereto information concerning the difference between the measured volume and the desired value.
- 10 - If the device is intended for a pipette whose piston is actuated by a motor, the microprocessor is programmed to control said motor such that the aspirated volume corresponds to the desired value.
- The device is a module that can be fitted to an existing pipette.

The invention also concerns a pipette integrating a verification device as previously defined.

- 15 The invention finally concerns a control and recording unit for managing a plurality of pipettes fitted with the verification device disclosed hereinbefore. This unit includes a computer that can be reduced, more simply, to a microprocessor device dedicated to this function, and a transceiver capable of making the computer communicate with the transceiver of each of the
- 20 pipettes.

Advantageously, the computer of this unit is programmed such that the following operations are carried out:

- sending the protocol of the pipetting operations to be carried out to each pipette;
- 25 - recording the performance of each pipette;
- recording the performance of the operator; and
- guiding the operator during a series of pipetting operations.

Brief Description of the Drawings

Other features and advantages of the present invention will appear from the following description, made with reference to the annexed drawing, in

30 which:

- Figure 1 is a schematic diagram of a pipette according to the invention and the control and recording unit to which it is connected;
- Figure 2 shows the programming logic of the pipette and the unit; and
- Figure 3 illustrates an alternative embodiment of the mechanical part of the pipette of Figure 1.

Detailed Description of Preferred Embodiments

The pipette shown in Figure 1 includes, in a conventional manner, a cylindrical chamber 10 into which a manually actuated piston 11 can slide. A seal 12 seals the contact between cylinder 10 and piston 11. Cylinder 10 is extended, at its base, by a shaft 13, whose end is provided with a removable conical dispensing tip 14. Finally, a counter 15 allows the operator to determine the volume of liquid to be dispensed. The travel of piston 11 will thus be automatically determined to follow this instruction.

Piston 11 can also be actuated by a motor, which replaces the action exerted manually by the operator.

The peculiarity of this pipette lies in the fact that it is provided with a verification module 16, which, in the example shown, occupies the extension of cylinder 10 and includes:

- a sensor 17 for supplying an air or any other fluid pressure measurement at two points of shaft 13 and a measurement of its temperature;
- a microprocessor 18 supplying, from said measurements, an indication of the volume of liquid aspirated into – or dispensed by – shaft 13, verifying that this volume corresponds to the desired volume and generating an indication relating to said verification;
- a communication interface 19 with the operator, which includes an LCD display 20, an acoustic alarm 21, a control button 22 and a transceiver 23, and

- a battery or accumulator 24 used to supply electric power to the module.

Sensor 17 essentially includes two chambers inserted in series, via a fluid restrictor, on the path of the fluid that flows into the shaft and provided
5 with an elastically deformable wall. Two electromechanical transducers respectively associated with the elastic wall of each chamber supply an electric signal representative of the pressure prevailing therein. A temperature sensor is arranged in proximity to the restrictor. This device is disclosed in document WO 02/071001 to which reference can be made for a complete
10 description.

Finally, transceiver 23 communicates, at short distance, outside the pipette, with another transceiver 25 associated with a computer 26, which form a central control and recording unit capable of managing a plurality of pipettes. The word "computer" used in the present document can also
15 designate any microprocessor device dedicated to the unit. The communication function between the pipettes and the central unit is achieved by any appropriate means known to those skilled in the art, such as hard-wired, infrared or radio (IEEE 802.15 or Bluetooth) transmissions.

According to the present invention, verification module 16 can either
20 form an integral part of the pipette, or be added to a conventional existing pipette. In the first case, only sensor 17 has to be placed along shaft 13, the other components being able to be incorporated in the body of the pipette and interconnected by any means available to those skilled in the art. In the second case, module 16 can either be inserted between the end of shaft 13
25 and its tip 14, or be incorporated in an assembly linking together piston 11 and shaft 13.

Reference will now be made to Figure 2, which describes the main operations carried out by microprocessor 18 of the pipette (on the right) and the external computer 26 (on the left).

30 When the operator wishes to carry out a series of liquid sampling and deposits, he begins, at 27, on computer 26, by identifying himself and indicating the time and date of his intervention, then by specifying, for example, the following parameters:

- the type and Identification number of the pipette;
- the dispensing protocol: number and volume of deposits to be carried out;
- the accepted tolerances.

5 Fewer parameters or more parameters may, of course, be specified.

Once the Identified pipette has been switched on using control button 22, the command can be given, at 28, to start operations. Computer 26 then sends the necessary instructions to the pipette, at 29.

These Instructions are received, at 30, by microprocessor 18 of the
10 pipette, which is then ready to operate.

After having adjusted counter 15 to the value of the volume to be dispensed, the operator then, in a conventional manner, takes a sample of the liquid, which takes place, by aspiration, in tip 14 of the pipette.

During this operation, microprocessor 18 receives from sensor 17
15 signals representative of the temperature and pressures in its two chambers. These three items of information allow it to calculate, at 31, the fluid flow rate into shaft 13, then, by integration, the volume of liquid aspirated into its tip 14.

The next operations are, at 32, comparison of the measured volume with the desired value received from the computer, then, at 33, display on
20 LCD 20 of a message indicating that the aspirated volume is – or is not – within the imposed tolerance limits.

If the desired value has been respected, the operator can then actuate his pipette to eject the liquid into the target intended therefor. If, conversely, the desired value has not been respected, acoustic alarm 21 is actuated.

25 Microprocessor 18 also sends to the computer, at 34, the result of the comparison, which is received at 35 then processed, at 36, so as to carry out a quality check in accordance with the rules of the "Good Laboratory and Manufacturing Processes".

Typically, the information elaborated and stored at 36 by computer 26
30 for a determined pipette are as follows (non exhaustive list):

- respect for the tolerances for each aspirated volume;
- standard deviation for a set of operations;
- variation coefficient for a set of operations;

- number of operations since the last maintenance service;
- number of operations until the next maintenance service;
- measured temperature for each operation;
- calibration history;
- 5 - percentage of failures;
- percentage of failures for identified operator;
- percentage of minor failures (slight limit violation requiring calibration)
- percentage of major failures (large limit violation due to
- 10 premature removal of the tip during suction or obstruction of the tip, other pipetting failure).

The next operation, at 37, is to determine whether the operation is a success or failure.

In the event of a failure, computer 26 sends the pipette, at 38, the
15 command, received at 30, to remedy the defect that caused the failure and to take another sample of liquid.

When the operation has been successful, computer 26 determines, at 39, whether the operations defined in the protocol have finished.

If this is not the case, computer 26 sends the pipette, at 40, the
20 command, received at 30, to continue operations. If, conversely, the protocol has finished, the computer returns, to 27 to begin a new series of liquid sampling and deposits.

In the case of a pipette whose piston is driven by an actuator, such as a motor, the pipette microprocessor 18 may optionally use the result of its
25 comparison 32 between the measured volume and the desired value to carry out, at 41, enslavement of the actuator which will thus drive the piston such that its travel allows the volume of liquid imposed by the desired value to be aspirated.

Reference will be made, in conclusion, to the alternative embodiment of
30 Figure 3 in which those elements common to those of Figure 1 are designated by the same reference numerals. In this case, piston 11 is extended by a portion of smaller diameter 42, which slides into the upper part of shaft 13.

Sealing is then achieved via a seal 43. This variant gives the pipette greater sensitivity to the movements of the piston.

Thus, there is proposed an intelligent pipette design, provided with a device for verifying its operations and benefiting from the assistance of a
5 central unit that controls and monitors it. All of the requirements of a modern and efficient quality system are thus satisfied.

Needless to mention that the design of the invention can apply both to single shaft pipettes and multiple shaft pipettes.